

### **IN THE CLAIMS**

This complete listing of the pending claims replaces all previous listings of the claims.

1. (withdrawn, currently amended) A method for in vitro detection of acute generalized inflammatory conditions (SIRS) in humans, comprising:

isolating ~~of~~ sample RNA from a sample of body fluids from a ~~mammal~~ human suspected of having SIRS;

labelling ~~of~~ the sample RNA, and/or at least one DNA being a gene or gene fragment specific for sepsis, with a detectable label [[.]],

contacting the sample RNA with the DNA under hybridization conditions;

contacting control sample RNA representing a control for non-pathologic conditions~~[[.]]~~ with at least one DNA~~[[.]]~~ under hybridization conditions, wherein ~~whereby~~ the DNA is a gene or gene fragment specific for SIRS, and wherein at least one of the control sample RNA and the DNA are labeled with a detectable label;

performing a quantitative detection of the label signals of the hybridized sample RNA and hybridized control sample RNA; and

comparing the quantitative data of the label signals; and

in the case that in order to determine whether the genes or gene fragments specific for SIRS are more expressed in the sample than in the control sample, diagnosing the ~~mamal~~ as having SIRS or less.

2. (currently amended) A method for in vitro diagnosis ~~detection~~ of sepsis and/or sepsis-like conditions in humans, comprising:

isolating ~~of~~ sample RNA from a sample of body fluids from a ~~mammal~~ human suspected of having sepsis or a sepsis like condition;

labelling ~~of~~ (a) the sample RNA, and/or (b) at least one DNA being a gene or gene fragment specific for sepsis, with a detectable label [[.]];

contacting the sample RNA with the DNA under hybridization conditions;

contacting control sample RNA representing a control for non-pathologic conditions~~[[.]]~~ with at least one DNA~~[[.]]~~ under hybridization conditions, wherein ~~whereby~~ the DNA is a gene or

gene fragment specific for sepsis and/or sepsis-like conditions, and wherein at least one of the control sample RNA and the DNA are labeled with a detectable label;

performing a quantitative detection of the label signals of the hybridized sample RNA and hybridized control sample RNA; and

comparing the quantitative data of the label signals; and

in the case that in order to determine whether the genes or gene fragments specific for sepsis and/or sepsis-like conditions are significantly over- or under- more expressed in the sample than in the control sample, diagnosing the mamal as having sepsis and/or a sepsis-like condition or less.

3. (withdrawn, currently amended) A method for in vitro detection of severe sepsis in humans, comprising:

isolating of sample RNA from a sample of body fluids from a mammal human suspected of having severe sepsis;

labelling of the sample RNA, and/or at least one DNA being a gene or gene fragment specific for sepsis, with a detectable label [,.];

contacting the sample RNA with the DNA under hybridization conditions;

contacting control sample RNA representing a control for non-pathologic conditions[,.] with at least one DNA[,.] under hybridization conditions, wherein whereby the DNA is a gene or gene fragment specific for severe sepsis, and wherein at least one of the control sample RNA and the DNA are labeled with a detectable label;

performing a quantitative detection of the label signals of the hybridized sample RNA and hybridized control sample RNA; and

comparing the quantitative data of the label signals; and

in the case that in order to determine whether the genes or gene fragments specific for severe sepsis are significantly over- or under- more expressed in the sample than in the control sample, diagnosing the mamal as having severe sepsis or less.

4. (currently amended) The method of claim 2 [1], wherein echaracterized in that the control RNA is hybridized with the DNA before the measurement of the sample RNA and the label signals

of the control RNA/DNA-complex is gathered and, optionally ~~if necessary~~, recorded in form of a calibration curve or table.

5. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ unchanged genes which show the same expression level in healthy patients as well as in patients with sepsis and/or sepsis-like symptoms from sample and/or control RNA are used as reference genes for the quantification.
6. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ mRNA is used as sample RNA.
7. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the DNA is arranged, ~~particularly~~ immobilized, on predetermined areas on a carrier in the form of a microarray.
8. (withdrawn, currently amended) The method of claim 1, wherein ~~characterized in that~~ the method is used for at least one of:
  - ~~for~~ early detection by means of differential diagnostics,
  - ~~for~~ control of the clinical and therapeutic progress, ~~f~~
  - ~~or~~ the individual risk evaluation in patients,
  - ~~for~~ the evaluation whether the patient will respond to a specific treatment, and
  - ~~as well as for~~ post mortem diagnosisof SIRS and/or sepsis and/or severe sepsis and/or systemic infections and/or septic conditions and/or infections.
9. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the sample is selected from the following group: body fluids, in particular are selected from the group consisting of blood, liquor, urine, ascitic fluid, seminal fluid, saliva, puncture fluid, cell content, and ~~or a mixtures~~ thereof.

10. (currently amended) The method of claim 9 ~~[[1]]~~, wherein ~~characterized in that~~ cell samples are subjected a lytic treatment, if necessary, in order to free their cell contents.
11. (canceled)
12. (currently amended) The method of claim 2 ~~[[1]]~~, wherein ~~characterized in that~~ the gene or gene segment specific for SIRS is selected from the group consisting of ~~SEQUENCE ID No. SEQ ID NO: III.1 to SEQUENCE ID No. SEQ ID NO: III.4168~~, as well as gene fragments thereof with 5-2000 or more, ~~preferably 20-200, more preferably 20-80~~ nucleotides.
13. (currently amended) A method for in vitro diagnosis of sepsis and/or sepsis-like conditions in humans, comprising:  
isolating of sample RNA from a sample of body fluids from a human suspected of having sepsis or a sepsis like condition;  
labelling the sample RNA, and/or at least one DNA being a gene or gene fragment specific for sepsis, with a detectable label;  
contacting the sample RNA with the DNA under hybridization conditions;  
contacting control sample RNA representing a control for non-pathologic conditions with at least one DNA under hybridization conditions, wherein the DNA is a gene or gene fragment specific for sepsis and/or sepsis-like conditions, and wherein at least one of the control sample RNA and the DNA are labeled with a detectable label;  
performing a quantitative detection of the label signals of the hybridized sample RNA and hybridized control sample RNA;  
comparing the quantitative data of the label signals; and  
in the case that the genes or gene fragments specific for sepsis and/or sepsis-like conditions are significantly over- or under-expressed in the sample than in the control sample, diagnosing the human having sepsis and/or a sepsis-like condition, and  
The method of claim 2, characterized in that wherein the gene or gene segment specific for sepsis and/or sepsis-like conditions is selected from the group consisting of:

SEQ ID NO:	Patent Seq ID	Accession No
220	I.220	(AI540783)

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Amendment A

Response to Office Action dated 03/05/2009

303	I.303	(AI149693)
529	I.529	(AA280062)
754	I.754	(AA150160)
844	I.844	(AA035016)
1705	I.1705	(R70541)
2370	I.2370	(AI888493)
2449	I.2449	(AI821631)
2468	I.2468	(AI820576)
2481	I.2481	(AI811413)
2709	I.2709	(AI732517)
2831	I.2831	(AI675585)
2928	I.2928	(AI623567)
2948	I.2948	(AI613016)
3068	I.3068	(AI554111)
3079	I.3079	(AI539445)
3209	I.3209	(AI364529)
3268	I.3268	(AI343613)
3305	I.3305	(AI273261)
3317	I.3317	(AI281098)
3331	I.3331	(AI224886)
3399	I.3399	(AA868082)
3424	I.3424	(AA833528)
3433	I.3433	(AA812763)
3482	I.3482	(AI214494)
3508	I.3508	(AI221860)
3523	I.3523	(AI218498)
3624	I.3624	(AI217376)
3676	I.3676	(AI148246)
3765	I.3765	(AI041544)
3796	I.3796	(AI003843)
3873	I.3873	(AA947111)
3879	I.3879	(AA923246)
3881	I.3881	(AA923169)
3917	I.3917	(AA825968)
4060	I.4060	(AA708806)
4096	I.4096	(AA682790)
4122	I.4122	(AA478996)
4141	I.4141	(AA417348)
4268	I.4268	(AA417792)
4328	I.4328	(AA493225)
4450	I.4450	(AA495787)
4528	I.4528	(AA453996)
4609	I.4609	(AA412166)
4654	I.4654	(AA398757)
4695	I.4695	(AA035428)
4705	I.4705	(AA029887)

4937	I.4937	(W04695)
5265	I.5265	(H91663)
5338	I.5338	(H65331)
5418	I.5418	(R94894)
5542	I.5542	(H18649)
5567	I.5567	(H16790)
5647	I.5647	(H06263)
5779	I.5779	(R43301)
6018	I.6018	(R12411)
6200	I.6200	(T78484)
2393	I.2393	(A1866414)
2870	I.2870	(A1656486)
3760	I.3760	(A1023463)
2293	I.2293	(A1924733)
3704	I.3704	(A1147412)

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~~SEQUENCE ID No. I.1 to SEQUENCE ID No. I.6242~~, as well as gene fragments thereof with 5-2000 or more, preferably 20-200, more preferably 20-80 nucleotides.

14. (currently amended) The method of claim 3, wherein ~~characterized in that~~ the gene or gene segment specific for severe sepsis is selected from the group consisting of ~~SEQUENCE ID No. SEQ ID NO: II.1 to SEQUENCE ID No. SEQ ID NO: II.130~~, as well as gene fragments thereof with 5-2000 or more, preferably 20-200, more preferably 20-80 nucleotides.
15. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ at least 2 to 100 different cDNAs are used.
16. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ at least 200 different cDNAs are used.
17. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ at least 200 to 500 different cDNAs are used.
18. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ at least 500 to 1000 different cDNAs are used.

19. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ at least 1000 to 2000 different cDNAs are used.
20. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the cDNA ~~SEQUENCE ID No. SEQ ID NO: III.1 to SEQUENCE ID No. SEQ ID NO: III.4168, SEQUENCE ID No. SEQ ID NO: I.1 to SEQUENCE ID No. SEQ ID NO: I.6242 and SEQUENCE ID No. SEQ ID NO: II.1 to SEQUENCE ID No. SEQ ID NO: II.130~~ replaced by synthetic analoga as well as peptidonucleic acids.
21. (currently amended) The method of claim 20, wherein ~~characterized in that~~ the synthetic analoga of the listed genes comprise 5-100, ~~in particular approximately 70,~~ base pairs.
22. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ a radioactive label, in particular  $^{32}\text{P}$ ,  $^{14}\text{C}$ ,  $^{125}\text{I}$ ,  $^{155}\text{Eu}$ ,  $^{33}\text{P}$  or  $^3\text{H}$  is used as detectable label.
23. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ a non-radioactive label is used selected from ~~as detectable label, in particular~~ a color- or fluorescence label, an enzyme label or immune label, and/or quantum dots or a label with an electrically measurable signal characterized by at least one of, ~~in particular~~ the change in potential, and/or conductivity and/or capacity by hybridizations.
24. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the sample RNA and control RNA bear the same label.
25. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the sample RNA and control RNA bear different labels.
26. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the immobilized probes bear a label.

27. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the cDNA probes are immobilized on glass or plastics.
28. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the individual cDNA molecules are immobilized on the carrier material by means of a covalent binding.
29. (currently amended) The method of claim 2 [[1]], wherein ~~characterized in that~~ the individual cDNA molecules are immobilized onto the carrier material by means of adsorption selected from, in particular by means of electrostatic and/or dipole-dipole and/or hydrophobic interactions and/or hydrogen bridges.
30. (withdrawn, currently amended) A method for in vitro detection of SIRS in humans, comprising:  
isolating sample peptides from a sample of body fluids from a mammal human suspected of having SIRS;  
labelling of the sample peptides with a detectable label;  
contacting the labelled sample peptides with at least one antibody or its binding fragment, whereby the antibody binds a peptide or peptide fragment specific for SIRS;  
contacting ~~the~~ labelled control peptides originating from healthy subjects[[,]] with at least one antibody or its binding fragment immobilized on a carrier in the form of a microarray, whereby the antibody binds a peptide or peptide fragment specific for SIRS;  
performing a quantitative detection of the label signals of the sample peptides and the control peptides;  
comparing the quantitative data of the label signals in order determine whether the peptide or peptide genes or gene fragments specific for SIRS are more expressed in the sample than in the control, and  
in the case that the the peptide or peptide fragments specific for SIRS are significantly over- or under-expressed in the sample than in the control, diagnosing said human as afflicted with SIRS or less.



31. (withdrawn, currently amended) A method for in vitro detection of sepsis and/or sepsis-like conditions in humans, comprising:

isolating sample peptides from a sample of body fluids from a mammal human suspected of suffering from sepsis and/or sepsis-like conditions;

labelling of the sample peptides with a detectable label;

contacting ~~the~~ labelled sample peptides with at least one antibody or its binding fragment, whereby the antibody binds a peptide or peptide fragment specific for sepsis and/or sepsis-like conditions;

contacting ~~the~~ labelled control peptides stemming from healthy subjects[[, ]]with at least one antibody or its binding fragment immobilized on a carrier in the form of a microarray, whereby the antibody binds a peptide or peptide fragment specific for sepsis and/or sepsis-like conditions;

performing a quantitative detection of the label signals of the sample peptides and the control peptides; and

comparing the quantitative data of the label signals in order to ~~be able to~~ determine whether the peptide or peptide genes or gene fragments specific for sepsis and/or sepsis-like conditions are more expressed in the sample than in the control, and

in the case that the the peptide or peptide fragments specific for sepsis and/or sepsis-like conditions are significantly over- or under-expressed in the sample than in the control, diagnosing said human as afflicted with specific for sepsis and/or sepsis-like conditions or less.

32. (withdrawn, currently amended) A method for in vitro detection of severe sepsis in humans, comprising:

isolating sample peptides from a sample of body fluids from a mammal human suspected of suffering from severe sepsis;

labelling of the sample peptides with a detectable label;

contacting ~~the~~ labelled sample peptides with at least one antibody or its binding fragment, whereby the antibody binds a peptide or peptide fragment specific for severe sepsis;

contacting ~~the~~ labelled control peptides stemming from healthy subjects~~[[, ]]~~with at least one antibody or its binding fragment immobilized on a carrier in the form of a microarray, whereby the antibody binds a peptide or peptide fragment specific for severe sepsis;

performing a quantitative detection of the label signals of the sample peptides and the control peptides; and

comparing the quantitative data of the label signals in order to determine whether the peptide or peptide ~~genes or gene~~ fragments specific for severe sepsis are more expressed in the sample than in the control, and

in the case that the the peptide or peptide fragments specific for severe sepsis are significantly over- or under-expressed in the sample than in the control, diagnosing said human as afflicted with severe sepsis or less.

33. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the antibody is immobilized on an array in form of a microarray.
34. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ it is formed as immunoassay.
35. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the method is used for at least one of:
- ~~for~~ early detection by means of differential diagnostics,
  - ~~for~~ control of the clinical and therapeutic progress, ~~f~~
  - ~~or~~ the individual risk evaluation in patients,
  - ~~for~~ the evaluation whether the patient will respond to a specific treatment, and
  - ~~as well as for~~ post mortem diagnosis
- of SIRS and/or sepsis and/or severe sepsis and/or systemic infections and/or septic conditions and/or infections.

36. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the body fluid sample is selected from the following group: ~~body fluids, in particular~~ blood, liquor, urine, ascitic fluid, seminal fluid, saliva, puncture fluid, cell content, and ~~or a mixtures~~ thereof.
37. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ cell samples are subjected a lytic treatment, if necessary, in order to free their cell contents.
38. (canceled).
39. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the peptide specific for SIRS is an expression product of a gene or gene fragment selected from the group consisting of ~~SEQUENCE ID No.~~ SEQ ID NO: III.1 to ~~SEQUENCE ID No.~~ SEQ ID NO: III.4168, as well as gene fragments thereof with 5-2000 nucleotides ~~or more, preferably 20-200, more preferable 20-80 nucleotides.~~
40. (withdrawn, currently amended) The method of claim 31, wherein ~~characterized in that~~ the peptide specific for sepsis and/or sepsis-like conditions is an expression product of a gene or gene fragment selected from the group consisting of ~~SEQUENCE ID No.~~ SEQ ID NO: I.1 to ~~SEQUENCE ID No.~~ SEQ ID NO: I.6242, as well as gene fragments thereof with 5-2000 nucleotides ~~or more, preferably 20-200, more preferable 20-80 nucleotides.~~
41. (withdrawn, currently amended) The method according to one of claim 32, wherein ~~characterized in that~~ the peptide specific for severe sepsis is an expression product of a gene or gene fragment selected from the group consisting of ~~SEQUENCE ID No.~~ SEQ ID NO: II.1 to ~~SEQUENCE ID No.~~ SEQ ID NO: II.130, as well as gene fragments thereof with 5-2000 ~~or more, preferably 20-200, more preferable 20-80 nucleotides.~~
42. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ at least 2 to 100 different peptides are used.

43. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ at least 200 different peptides are used.
44. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ at least 200 to 500 different peptides are used.
45. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ at least 500 to 1000 different peptides are used.
46. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ at least 1000 to 2000 different peptides are used.
47. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ a radioactive label selected from, in particular  $^{32}\text{P}$ ,  $^{14}\text{C}$ ,  $^{125}\text{I}$ ,  $^{155}\text{Eu}$ ,  $^{33}\text{P}$  and  $^3\text{H}$  ~~or~~ is used as detectable label.
48. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ a non-radioactive label is used as detectable label, ~~in particular~~ selected from a color- or fluorescence label, an enzyme label or immune label, and/or quantum dots or a label capable of being detected as an electrically measurable signal, ~~in particular~~ selected from the change in potential, and/or conductivity and/or capacity by hybridizations.
49. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the sample peptides and control peptides bear the same label.
50. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the sample peptides and control peptides bear different labels.
51. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the probes used are peptides to which labelled antibodies are bound, which cause a change of signal of the labelled antibodies by change of conformation when binding to the sample peptides.

52. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the peptide probes are immobilized on glass or plastics.
53. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the individual peptide molecules are immobilized onto the carrier material by means of a covalent binding.
54. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the individual peptide molecules are immobilized on the carrier material by means of adsorption, ~~in particular~~ by means of electrostatic and/or dipole-dipole and/or hydrophobic interactions and/or hydrogen bridges.
55. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the individual peptide molecules are detected by means of monoclonal antibodies or their binding fragments.
56. (withdrawn, currently amended) The method of claim 30, wherein ~~characterized in that~~ the determination of individual peptides by means of immunoassay or precipitation assay is carried out using monoclonal antibodies.
57. (cancelled)
58. (cancelled)
59. (cancelled)
60. (new) The method of claim 2, wherein the gene or gene segment specific for sepsis and/or sepsis-like conditions is selected from the group consisting of:

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Amendment A  
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6250	II.8	(BC018761)
6251	II.9	(XM_030906)
6259	II.17	(NM_001562)
6267	II.25	(NM_001560)
6271	II.29	(XM_036107)
6297	II.55	(XM_041847)
6314	II.72	(NM_001511)
6327	II.85	(XM_007258)

as well as gene fragments thereof with 5-2000 nucleotides.